REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 C.F.R. § 1.116

REMARKS

Upon entry of this amendment, claims 40, 41, 45, 47, 54, 56, 57, 59, 62-63, 68, 70, 72, 75, 76, 78, and 80-91, 93, 121-128, 130, and 139 will be pending in the present application. Claims 92, 94-120, 129, and 131-138 are canceled herein without prejudice to the prosecution of the subject matter contained therein at a later date. Claims 45, 54, 56, 57, 59, 62, 63, 70, 75, 78, 80, and 81 are amended herein. The amendments to claims 45, 54, 62, 75, and 78 reciting CAI antigen polypeptide fragments including at least one of the amino acid sequences of SEQ ID NO:9, SEQ ID NO:10, or six contiguous asparagine residues is supported by the specification, for example, in Figure 4. No new matter has been introduced by way of this amendment.

Preliminarily, Applicants note with appreciation the indication of allowability of claims 40, 41, and 72 and withdrawal of the prior objections and rejections as noted.

Applicants further note with appreciation the favorable consideration of the Supplemental Information Disclosure Statement submitted September 12, 2002. Applicants submit herewith a Supplemental Information Disclosure Statement for consideration by the Examiner.

I. Claims 81, 84-91, 93, 121-123, 126-128, 130, and 139 should be rejoined.

It is asserted that claims 81, 84-123, and 126-139 are drawn to non-elected inventions. Applicants note that claims 92, 94-120, 129, and 131-138 have been canceled without prejudice. Applicants traverse the withdrawal of pending claims 81, 84-91, 93, 121-123, 126-128, 130, and 139.

Applicants have elected claims drawn to polypeptides of *Helicobacter pylori* CAI antigen, immunogenic compositions comprising the same, and methods of preparing the immunogenic compositions. The nonelected invention encompasses methods of treating an individual infected with *Helicobacter pylori.* Claims 81, 84-91, 93, 121-123, 126-128, 130, and 139 recite *Helicobacter pylori* polypeptides derived from the CAI antigen. Accordingly, those claims should be rejoined.

Moreover, Applicants assert that rejoinder of claims 81, 84-91, 93, 121-123, 126-128, 130, and 139 would impose no serious burden on the examiner. A search of *Helicobacter pylori* CAI antigen polypeptides as presented in claims 40, 41, 45, 47, 68, 72, 75, 76, 82, 83, 124, and 125 would encompass within its scope a search of the polypeptides set forth in claims 81, 84-91, 121-123, 126-168, 130, and 139. Accordingly, Applicants request consideration of claims 81, 84-91, 121-123, 126-128, 130, and 139 on their merits.

At a minimum, Applicants assert that the claims should be rejoined to the extent they recite polypeptides of *Helicobacter pylori* CAI antigen having at least ten amino acids or encoded by at least thirty nucleotides.

II. Claims 45, 47, 54, 56, 57, 59, 62, 63, 68, 70, 75, 76, 78, and 80 are adequately supported by the specification as filed.

Claims 45, 47, 54, 56, 57, 59, 62, 63, 68, 70, 75, 76, 78, and 80 are rejected under 35 U.S.C. § 112, first paragraph for alleged lack of written descriptive support. Applicants disagree. Nonetheless, to advance prosecution of the present application, Applicants have omitted the phrase "substantially noncytotoxic" from the claims.

The identifying characteristics of the polypeptides set forth in claims 45, 47, 54, 56, 57, 59, 62, 63, 68, 70, 75, 76, 78, and 80 are sufficient to show possession of the claimed invention to one of ordinary skill in the art. As the claims are adequately supported by the application as filed, Applicants request withdrawal of the rejection.

III. Claims 45, 47, 54, 56, 57, 59, 62, 63, 68, 70, 75, 76, 78, and 80 satisfy the requirements of 35 U.S.C. § 112, second paragraph.

Claims 45, 47, 54, 56, 57, 59, 62, 63, 68, 70, 75, 76, 78, and 80 are rejected for alleged indefiniteness in the recitation of the phrase "substantially noncytotoxic." Applicants note that the phrase at issue has been omitted from claims 45, 54, 57, 62, 63, 70, 75, and 78.

IV. Claims 45, 47, 48, 54, 56, 57, 59, 62, 63, 68, 70, 75, 76, 78, 80, 82, 83, 124, and 125 are enabled by the specification.

Claims 45, 47, 48, 54, 56, 57, 59, 62, 63, 68, 70, 75, 76, 78, 80, 82, 83, 124, and 125 are rejected for alleged lack of enablement under 35 U.S.C. § 112, first paragraph. Applicants disagree.

The enablement requirement of 35 U.S.C. § 112, first paragraph, mandates that the specification teach those in the art how to make and use the claimed invention without undue experimentation. *See In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) (citing *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916)). The test of enablement is not whether any experimentation is necessary but, whether, if experimentation is necessary, it is undue. *See In re Angstadt*, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). Moreover, the fact that

experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *See Wands*, 8 U.S.P.Q.2d at 1404.

The factors to be considered in determining whether any necessary experimentation is undue include:

i. the breadth of the claims;
ii. the nature of the invention;
iii. the state of the prior art;
iv. the level of one of ordinary skill;
v. the level of predictability in the art;
vi. the amount of direction provided by the inventor;
vii. the existence of working examples; and
viii. the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Id. (citing *Ex parte Forman*, 230 U.S.P.Q. 546, 547 (Bd. Pat. App. & Int. 1986)). Any conclusion of nonenablement must be based on the evidence as a whole. *See id.* In order to make a rejection, the examiner has the burden to establish a reasonable basis to question the enablement provided for the claimed invention. *See In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. *See In re Marzocchi*, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971). The burden then shifts to the applicant to provide persuasive arguments, supported by suitable proofs where necessary, that one skilled in the art would be able to make and use the claimed invention using the application as a guide. *See In re Brandstadter*, 179 U.S.P.Q. 286, 294 (C.C.P.A. 1973).

Applicants submit that the skilled artisan would be able to make and use the claimed invention using the application as a guide.

The Examiner alleges that

> Contrary to Applicants' assertion, the instant specification does not serve as a 'guide' enabling one of skill in the art to produce a non-fragmented whole CAI, CT or HSP antigen of *H. pylori* that possesses the following required functions: a) substantial non-cytotoxicity; b) ability to induce antibodies specific to *H. pylori*; c) ability to serve as a prophylactic or therapeutic vaccine either alone or in combination.

Office Action at 6. Applicants disagree.

The specification need only disclose one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claims to satisfy the enablement requirement. *In re Fischer*, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970).

> For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.

MPEP § 2164.02.

The fact that some experimentation may be required is not fatal; the question is whether the experimentation is undue. *See Wands*, 8 U.S.P.Q.2d at 1404. Moreover, "an extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re Colianni*, 561 F.2d 220, 224 (C.C.P.A. 1977). Even "a

considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Wands*, 8 U.S.P.Q.2d at 1404.

Although Applicants disagree with the rejection, Applicants have omitted the phrase "substantially noncytotoxic" from the claims in reference to CAI, Hsp, and CT polypeptides.

Applicants further submit that claims reciting *Helicobacter pylori* polypeptides having the ability to induce *H. pylori* antigen-specific antibodies are enabled by the specification. Nonetheless, in order to advance prosecution of the application, Applicants have amended the claims to recite polypeptides that are immunologically identifiable by antibodies that react specifically with *Helicobacter pylori* CAI antigen, Hsp, or CT. Support for these amendments is found throughout the specification as filed. For example, the specification discloses the use of a full length CAI antigen protein to produce a mouse serum having specificity therefor. *See, e,g.,* specification at 50, line 29 to 51, line 1. The serum was subsequently used to detect immunologically identifiable clones. *See, e.g.,* specification at 51, lines 3-12. Similarly, *Helicobacter pylori* Hsp-specific antibodies were used to detect polypeptides that are immunologically identifiable with *Helicobacter pylori* Hsp, including fusion proteins and a 58 kDa protein from whole cell extracts of several strains of *H. pylori*. *See, e.g.,* specification at 57, lines 14-33; 58, line 34 to 59, line 6. In addition, the specification discloses the preparation of antisera against the *Helicobacter pylori* cytotoxin and the use of the antisera to detect polypeptides immunologically identifiable with the *H. pylori* CT. *See, e.g.,* specification at 45, line 26 to 46, line 6.

The Examiner has further alleged that the prophylactic and therapeutic vaccines of the invention are not enabled by the specification. Applicants disagree. Nonetheless, Applicants have amended claims 54, 56, 57, 59, 62, 63, 70, 78, and 80 to recite immunogenic compositions. The amendment is fully supported by the specification as filed. *See, e.g.,* Specification at 14, lines 31-34 (defining "immunogenic" as the ability of a polypeptide to cause a humoral or cellular immune response); 40, line 16 to 41, line 17 (defining the immunogenic compositions of the invention). Accordingly, Applicants request reconsideration and withdrawal of the enablement rejection under 35 U.S.C. § 112, first paragraph.

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CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please contact the undersigned at 215-557-5908.

Respectfully submitted,

Date: February 26, 2003

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Attachments

Supplemental Information Disclosure Statement

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Please amend claims 45, 54, 56, 57, 59, 62, 63, 70, 75, 78, 80, and 81 as follows:

45. (Four times amended) A purified polypeptide comprising at least ten contiguous amino acids of SEQ ID NO:5, wherein said polypeptide includes at least one of the amino acid sequences selected from the group consisting of SEQ ID NO:9, SEQ ID NO:10, and six contiguous asparagine residues, which polypeptide is immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* CAI antigen [: (i) can be used to induce the production of antibodies to *Helicobacter pylori* CAI antigen, and (ii) is substantially noncytotoxic].

54. (Four times amended) [A prophylactic or therapeutic vaccine] An immunogenic composition comprising an immunologically effective amount of a recombinant polypeptide, which recombinant polypeptide: (i) comprises at least ten contiguous amino acids of SEQ ID NO:5, wherein said polypeptide includes at least one of the amino acid sequences selected from the group consisting of SEQ ID NO:9, SEQ ID NO:10, and six contiguous asparagine residues, and (ii) is immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* CAI antigen [can be used to induce the production of antibodies to *Helicobacter pylori* CAI antigen, and (iii) is substantially noncytotoxic].

56. (Four times amended) The [vaccine] immunogenic composition of claim 54 wherein said polypeptide comprises at least fifteen contiguous amino acids of SEQ ID NO:5.

57. (Four times amended) The [vaccine] immunogenic composition of claim 54 further comprising an immunologically effective amount of a second polypeptide, which second polypeptide: (i) comprises at least ten contiguous amino acids of *Helicobacter pylori* heat shock protein, and (ii) is immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* heat shock protein [can be used to induce the production of antibodies to *Helicobacter pylori* heat shock protein, and (iii) is substantially noncytotoxic].

59. (Four times amended) The [vaccine] immunogenic composition of claim 57 wherein said second polypeptide comprises at least fifteen contiguous amino acids of *Helicobacter pylori* heat shock protein.

62. (Four times amended) A method of preparing [a prophylactic or therapeutic vaccine] an immunogenic composition comprising bringing into association:

(1) an immunologically effective amount of a purified polypeptide, which polypeptide: (i) comprises at least ten contiguous amino acids of SEQ ID NO:5, wherein said polypeptide includes at least one of the amino acid sequences selected from the group consisting of SEQ ID NO:9, SEQ ID NO:10, and six contiguous asparagine residues, and (ii) is immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* CAI antigen [can be used to induce the production of antibodies to *Helicobacter pylori* CAI antigen, and (iii) is substantially noncytotoxic], and

(2) a pharmaceutically acceptable carrier.

63. (Four times amended) The method of claim 62 or 78 further comprising adding an immunologically effective amount of a second polypeptide, which second polypeptide: (i) comprises at least ten contiguous amino acids of *Helicobacter pylori* heat shock protein, and (ii) is immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* heat shock protein [can be used to induce the production of antibodies to *Helicobacter pylori* heat shock protein, and (iii) is substantially noncytotoxic].

70. (Three times amended) The [vaccine] immunogenic composition of claim 54, further comprising an immunologically effective amount of a second polypeptide, wherein said second polypeptide: (i) comprises at least ten contiguous amino acids of *Helicobacter pylori* cytotoxin (CT) protein, and (ii) [can be used to induce the production of antibodies to] is immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* cytotoxin[, and (iii) is substantially noncytotoxic].

75. (Twice amended) A recombinant polypeptide comprising at least ten contiguous amino acids of SEQ ID NO:5, wherein said polypeptide includes at least one of the amino acid

sequences selected from the group consisting of SEQ ID NO:9, SEQ ID NO:10, and six contiguous asparagine residues, which recombinant polypeptide is immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* CAI antigen [: (i) can be used to induce the production of antibodies to *Helicobacter pylori* CAI antigen, and (ii) is substantially noncytotoxic].

78. (Twice amended) A method of preparing [a prophylactic or therapeutic vaccine] an immunogenic composition comprising bringing into association:

(1) an immunologically effective amount of a recombinant polypeptide, which recombinant polypeptide: (i)comprises at least ten contiguous amino acids of SEQ ID NO:5, wherein said polypeptide includes at least one of the amino acid sequences selected from the group consisting of SEQ ID NO:9, SEQ ID NO:10, and six contiguous asparagine residues, and (ii) is immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* CAI antigen [can be used to induce the production of antibodies to *Helicobacter pylori* CAI antigen, and (iii) is substantially noncytotoxic], and

(2) a pharmaceutically acceptable carrier.

80. (Twice amended) The [vaccine] immunogenic composition of claim 70 wherein said second polypeptide comprises at least fifteen contiguous amino acids of *Helicobacter pylori* CT protein.

81. (Amended) An isolated immunogenic polypeptide comprising at least five contiguous amino acids from SEQ ID NO:5, wherein said polypeptide is immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* CAI antigen.

Please cancel claims 92, 94-120, 129, and 131-138 without prejudice to the prosecution of the subject matter contained therein at a later date.